TRIDENTATE COBALT COMPOUNDS

by

HARVEY DIEHL

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, in the University of Michigan.

1936

CONTENTS

Introduction

Theory and Definition of Terms 1
Requirements of a Tridentate Molecule 2

Experimental Part

Objectives, Methods and Difficulties 4
α, γ - Diaminobutyric Acid 4
α, β - Diaminopropionic Acid 5
Aspartic Acid 5
Aminomalonic Acid 5

Formation of Tridentate Compounds 6
Cobalt and α, β - Diaminopropionic Acid 6
Cobalt and Aspertic Acid 6

Experimental Details 7

Summary 20

Bibliography 21

ACKNOWLEDGEMENT

To Professor H. H. Willard for his constant help and encouragement I wish to express my sincere thanks and appreciation.

Harvey Diehl

Ann Arbor
August, 1936

INTRODUCTION

Theory and Definition of Terms

The term "chelate", proposed by Morgan(1) to designate organic molecules yielding ring systems with metal atoms, is derived from the Greek "kela", the great claw of the lobster and crustaceans, suggested by the caliper like character of these molecules.

The formation of these rings may involve primary or secondary valence. In subsequent papers Morgan used the expression "chelate rings" to cover all three types, that is, rings formed by two primary valences, one primary and one secondary valence, or two secondary valences.

With the discovery of molecules bearing three and four groups capable of associating with a single metal atom Morgan adopted the names "tridentate", literally, three-toothed, and "quadridentate", literally, four-toothed, for these compounds(2).

Because of the little attention this field has attracted the simple variation of acidic and coordinating groups in the polydentate molecules has escaped investigation. The following classification is, however, obvious:

A. Unidentate
   1. Either acidic or coordinating (groups held in the coordination sphere)

B. Bidentate
   1. Two acidic groups (SO_4^{--}, $C_2O_4^{--}$, etc.)
   2. One acidic, one coordinating (β - diketones, amino acids, dioximes, etc.)
   3. Two coordinating (ethylenediamine, dipyridyl, etc.)

C. Tridentate
   1. Three acidic
   2. Two acidic, one coordinating
   3. One acidic, two coordinating
   4. Three coordinating

D. Quadridentate
   1. Four acidic
   2. Three acidic, one coordinating
   3. Two acidic, two coordinating
   4. One acidic, three coordinating
   5. Four coordinating

and so on for quinqitdentate and sexadentate.

Of Class A thousands of examples are known, of Classes B1, B2, and B3 numerous examples exists, of Class C4 one example is known (see later) but of C1, C2, and C3 none has been recorded as being definitely one of these types. Of the quadridentate classes, members of class D3 only are known.

The purpose of this investigation is the preparation of members of Classes C2 and C3. The types of compounds produced should be strictly in accord with the coordination theory of Werner, the ionic character of the complexes formed being governed by the rule: the valence of the complex ion is equal to the valence of the central metal atom minus the number of acidic groups in the coordination sphere.

For a given metal, as the numbers of the acidic and the coordinating

(1) Numbers refer to bibliography.

groups comprising its coordination sphere are progressively changed, there is a corresponding variation in the charge carried by the complex ion. One step in the sequence is a non-ionic compound. Those non-electrolyte compounds which are also chelate in character are designated as "inner complex"* compounds and possess unusual properties. They are non-polar in nature, being insoluble in water but highly soluble in organic solvents, having striking colors widely different from the color of the normal salts of the metal, and having remarkable stability and usually a very well defined composition. These properties coupled with a low metal content make them important for analytical purposes.

Among the bidentate compounds, inner complexes exist only in the Class B2 and therefore only with metals whose coordination number (K.Z.) is twice the primary valence (P.V.). Fortunately this is the case with most of the common metals, for example, Cu, Ni, Mg, Pd^{++}, Pt^{++} (K.Z. = 4, P.V. = 2); Co, Ir, Fe, Al (K.Z. = 6, P.V. = 3).

Among the tridentate molecules inner complexes may result in classes C2 and C3, for example in C2 if K.Z. = 6 and P.V. = 4, or in C3 if K.Z. = 6 and P.V. = 2. Or taking a more general view:

	K.Z. = 6	K.Z. = 6
P.V. = 2	$[M^{++}\ (C3)_2]^\circ$	$[M^{++}\ (C2)_2]^{--}$
= 3	$[M^{+++}\ (C3)_2]^{+}$	$[M^{+++}\ (C2)_2]^{-}$
= 4	$[M^{++++}\ (Cv)_2]^{++}$	$[M^{++++}\ (C3)_2]^\circ$

where C2 and C3 represent the tridentate molecules. A number of metals have K.Z. = 6 and P.V. = 2 or 4, Pt^{++++}, Co^{++}, Fe^{++}, Zr^{++++}, Si^{++++}, Ti^{++++}; tridentate organic molecules if they could be found might yield inner complexes with these elements and be of great analytical value.

Requirements of a Tridentate Molecule

While the subtle relations of structure to specificity of an organic molecule for a metal have eluded explanation, the primary consideration in the formation of chelate rings is the number of members in the ring. Four and seven membered rings are known, but five and six membered rings are by far the most common and stable configurations. The five membered ring is somewhat favored because the angle at the metal atom is only 90°, whether the coordination number be four or six; but the other elements and their mode of linkage in the ring exert modifying influences which sensibly alter the configuration. For excellent discussions of this problem the reader is referred to Sidgwick(3) and Pfeiffer(4).

The union of a tridentate molecule with a metal atom involves the formation of a cage system the geometrical considerations of which are more easily grasped by the use of models. In preparing models, the relative sizes of the larger metal atom and the smaller carbon, nitrogen, and oxygen atoms and the distances between the atoms was taken into consideration; the assumption was made that the angles between the valences of the oxygen atom was 109° as in the tetrahedral carbon and nitrogen atoms.

The only tridentate molecule on record is the organic base α, β, γ - triaminopropane, $CH_2(NH_2)CH(NH_2)CH_2(NH_2)$ (abbreviated ptn) which

*The term "inner complex" has been loosely used by some authors to cover all chelate compounds; strictly the term refers only to those chelate compounds which are also non-electrolytes; the anomolous properties ascribed to "inner complexes" characterize only those chelate compounds which are non-ionic.

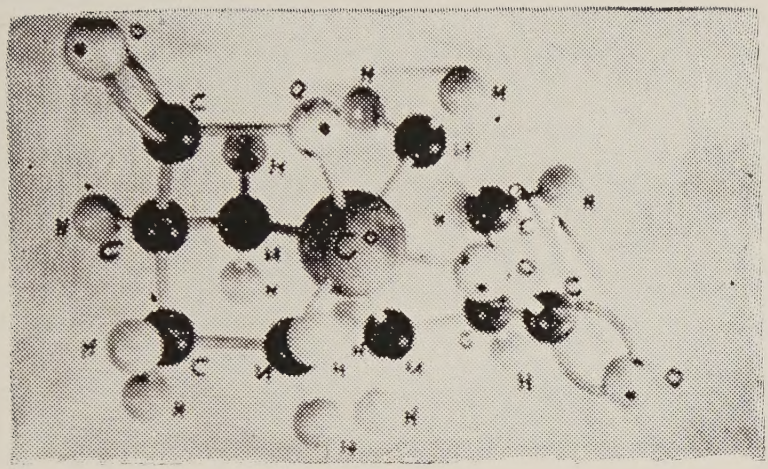

Figure 1

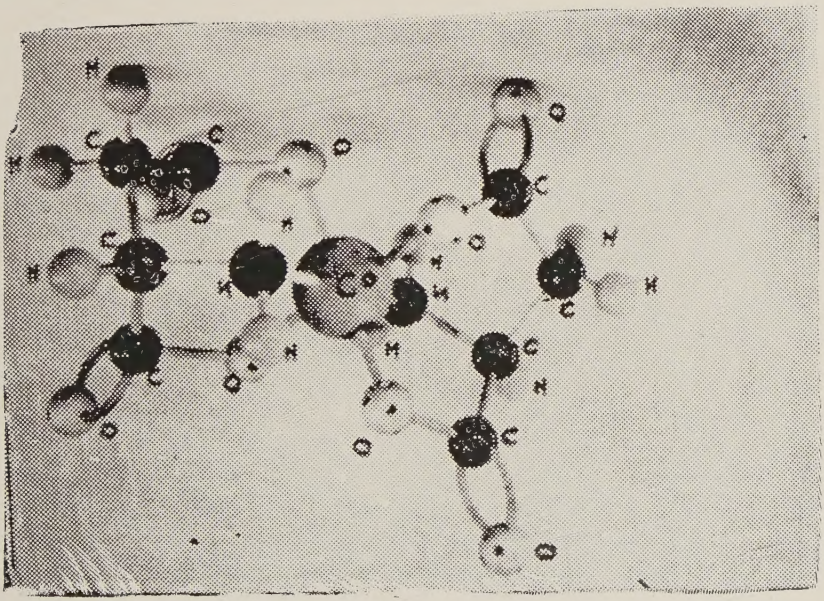

Figure 2

Digitized by the Internet Archive
in 2026

https://archive.org/details/IA41551510_0129

was shown by Mann (5,6) to occupy three positions of the coordination sphere around a metal atom; he prepared the complex ions

$$[Co^{+++}(ptn)_2]^{+++} \text{ and } [Ir^{+++}(ptn)_2]^{+++}$$

The ease with which the triaminopropane molecule cages with the metal atom was readily shown by models; but a very slight strain is required to close the system.

Obviously then for tridentate molecules having one acidic and two coordinating groups, or two acidic and one coordinating group, the number and arrangement of the atoms in α, β, γ -triaminopropane should be retained; assuming nitrogen and oxygen to have the same size and angular characteristics, the compounds which are immediately suggested are α, β-diaminopropionic acid, $CH_2(NH_2)CH(NH_2)COOH$, and aminomalonic acid, $HOOCCH(NH_2)COOH$. The model of the diaminopropionic acid-metal atom system is shown in Figure 1, in which two such molecules surround the octahedrally arranged metal of coordination number six.

The models further show that a four carbon chain bearing three associating groups is just as easily fitted about the metal atom, and again the obvious compounds are α, γ-diaminobutyric acid, $CH_2(NH_2)CH_2CH(NH_2)COOH$, and aspartic acid, $HOOCCH_2CH(NH_2)COOH$. A model illustrating the linkage of aspartic acid to metal of coordination number six is shown in Figure 2.

Other acidic and coordinating groups may be available for tridentate molecules but the simplest appear to be the amino acids mentioned.

EXPERIMENTAL PART

Objectives, Methods and Difficulties

Of the four acids α, γ-diaminobutric, α,β-diaminopropionic, aspartic and aminomalonic acid, which models indicate may serve as tridentate molecules, all four appear in the literature. The synthethic approach to these acids is widely different but in all cases quite involved. Good methods are available for the preparation of the diaminopropionic and aspartic acids but the preparation of the remaining two acids is beset with difficulties and the acids themselves have been but seldom studied.

As sources of trivalent cobalt for the formation of the complex compounds, the ammoniates, bromo-pentammino-cobalti bromide and carbonato-tetrammino-cobalti chloride, were prepared and some time spent on improving their syntheses.

α, γ - Diaminobutyric Acid

α, γ - Diaminobutyric acid was prepared by Emil Fischer(7) in 1901 but does not appear in the literature again. The method of synthesis employed by Fischer is outlined in Figure 3, scheme 1. Unable to obtain phthalimidoethyldiethyl malonate, first prepared by Aschan(8), in crystalline form, Fischer went on with the oily material obtained and in the next step, bromination, obtained a crystalline product, subsequent steps apparently also being satisfactory.

In this work, too, it was impossible to obtain phthalimidoethyldiethyl malonate in crystalline form and the oily material was therefore brominated.

Fischer's method was carefully followed, but several attempts yielded non-crystallizable products. The bromination was run under a variety of conditions on material prepared in various ways (see experimental details). The oily products obtained from these experiments yielded, on pursuing furthtr steps in Fischer's synthesis, hopelessly non-crystalline oils or small amounts of crystalline materials melting at temperatures widely different from those recorded.

Attention was then directed to the preparation of phthalimidoethyldieethyl malonate which involves the condensation of β-bromethyl phthalimide and sodium diethyl malonate A great number of variations and conditions affecting the reaction were tried with no improvement in product. Condensation was also attempted by fusion of β-bromethylphthalimide with solid sodium diethyl malonate; this also gave an oily product. This work was then dropped in favor of other possible syntheses.

Later a further study of this reaction appeared(9) in which the oily material was fractionated under vacuum; this work was promply repeated but the fractionation was so tedious and the yield of distilled material so low, that the preparation of the large amounts needed for the subsequent reactions appeared hopeless; bromination furthermore gave only oily material.

Other possible methods of synthesizing α, γ-diaminobutyric acid were devised and attempted. The first (Figure 3, scheme II), involving a Strecker synthesis, started from acrolein, the double bond of which had been modified by the addition of hydrochloric acid. The exceedingly disagreeable properties of acrolein coupled with the lack of adequate ventilation completely discouraged such an undertaking after a few preliminary experiments. A somewhat similar synthesis was carried out by Crawford and Kenyon(10).

Another possible method is analogeus to a procedure used by Fischer (11) for synthesizing α,ε-diaminocaproic acid: this involves (Figure 4, scheme III) the coupling of chloracetonitrile with sodium diethyl malon-

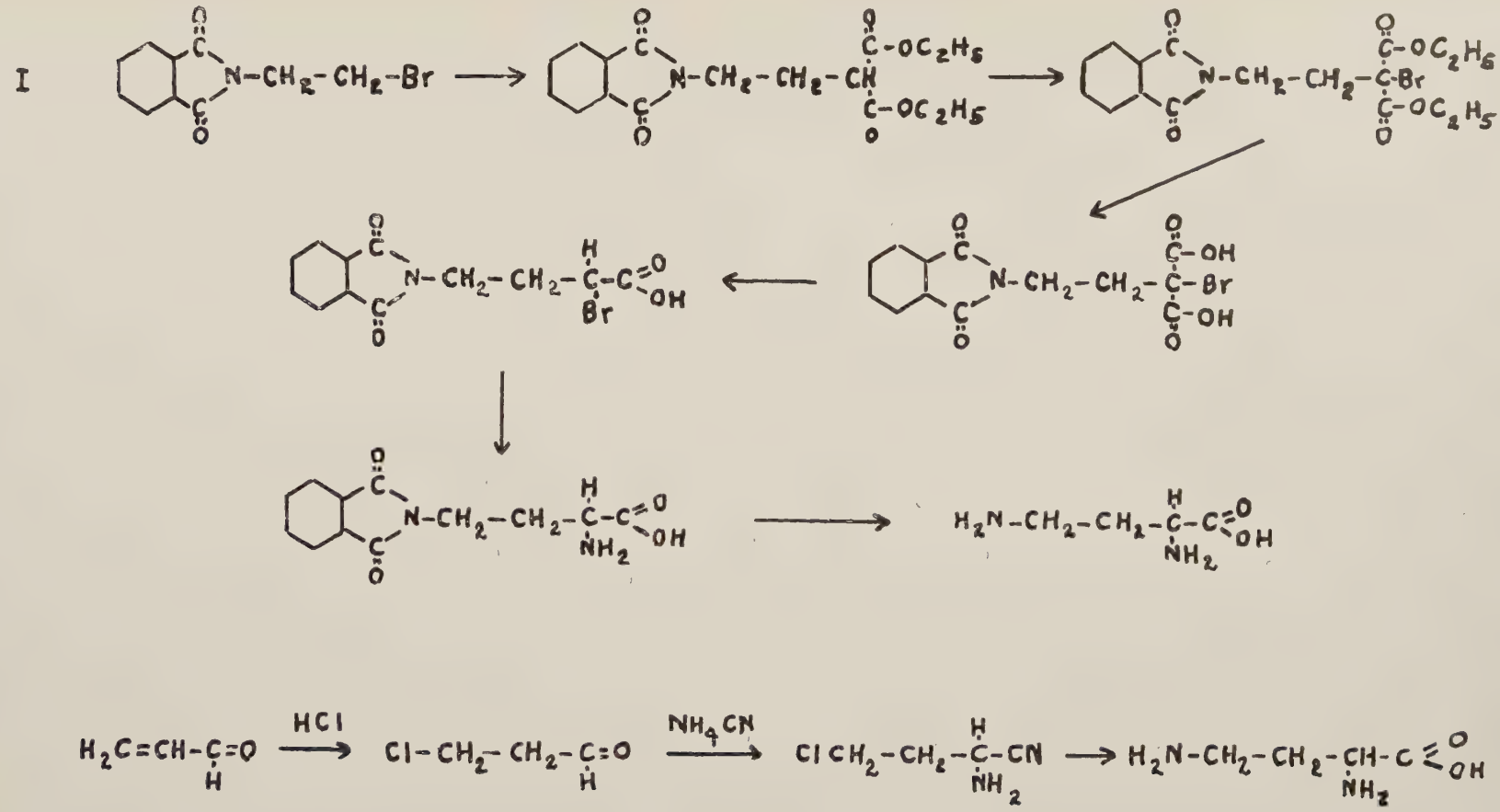

FIGURE 3

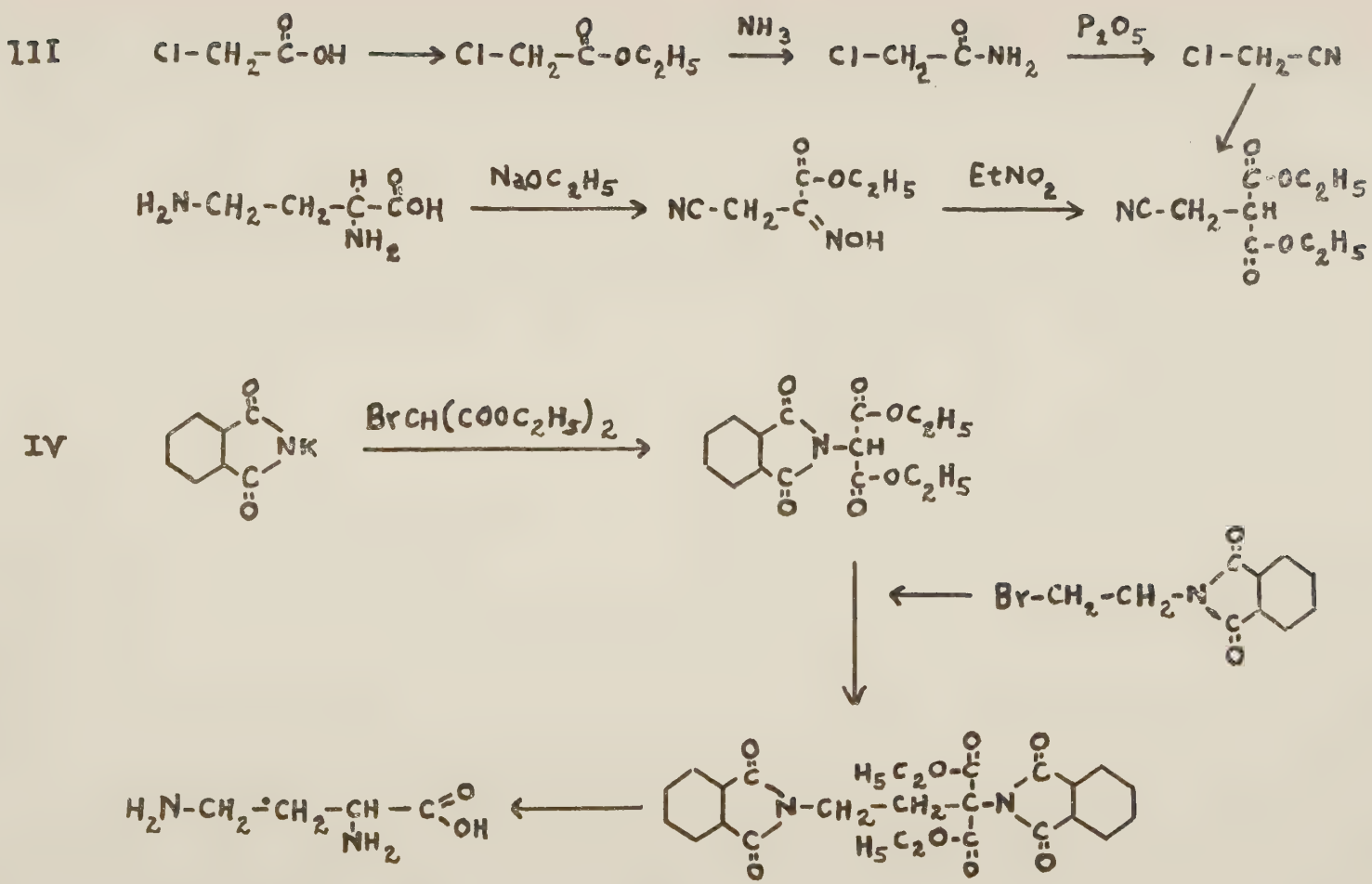
III
Cl-CH2-C(=O)-OH
Cl-CH2-C(=O)-OC2H5
NH3
Cl-CH2-C(=O)-NH2
P2O5
Cl-CH2-CN
H2N-CH2-CH2-CH(NH2)-C(=O)OH
NaOC2H5
NC-CH2-C(=NOH)-C(=O)OC2H5
EtNO2
NC-CH2-CH(C(=O)OC2H5)-C(=O)OC2H5
IV
NK
BrCH(COOC2H5)2
N-CH(C(=O)OC2H5)-C(=O)OC2H5
Br-CH2-CH2-N
H5C2O-C(=O)-CH2-CH2-C(=O)-OC2H5
H2N-CH2-CH2-CH(NH2)-C(=O)OH

FIGURE 4

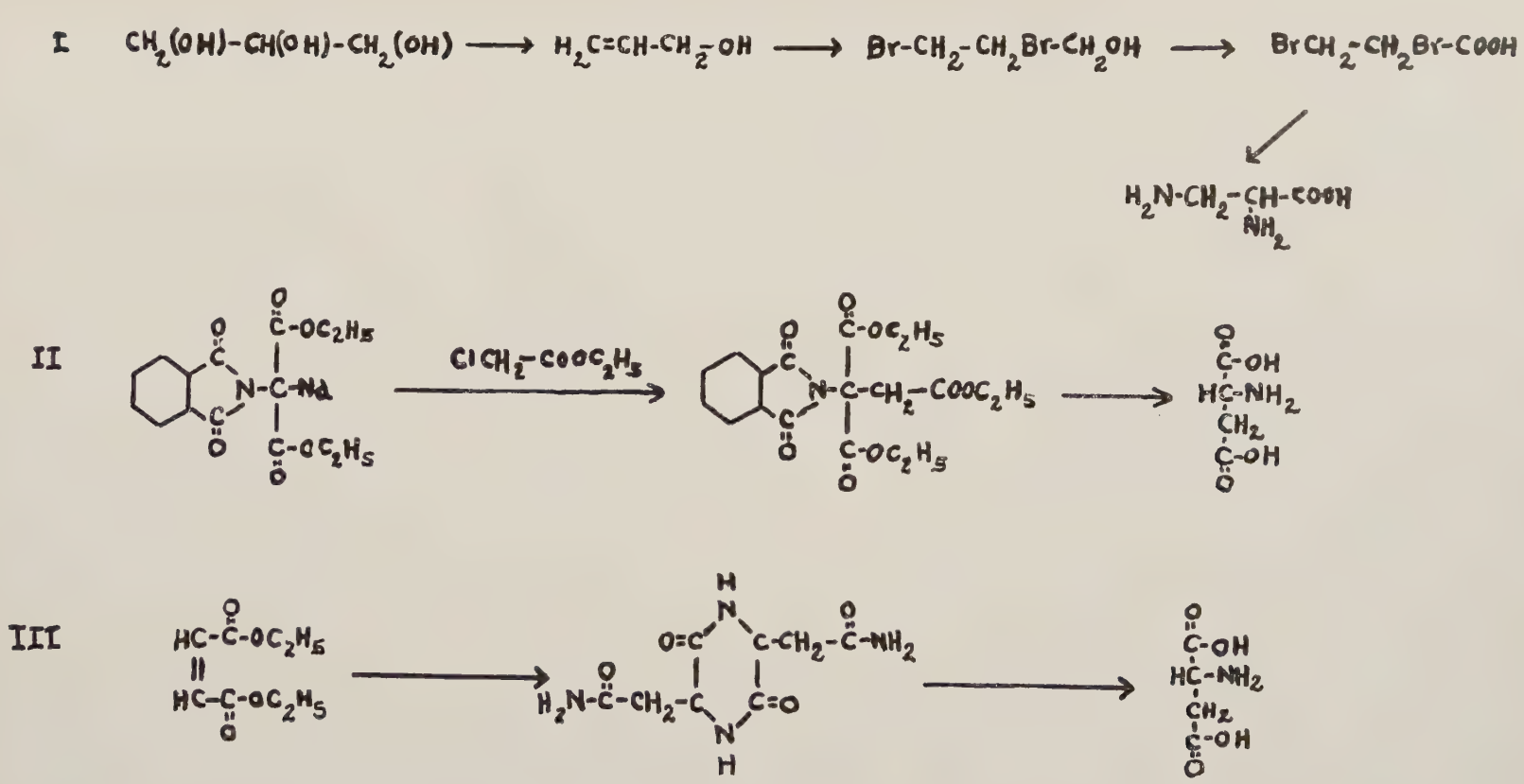
I
CH2(OH)-CH(OH)-CH2(OH)
H2C=CH-CH2-OH
Br-CH2-CH2Br-CH2OH
BrCH2-CH2Br-COOH
H2N-CH2-CH-COOH
NH2
II
ClCH2-COOC2H5
III

FIGURE 5

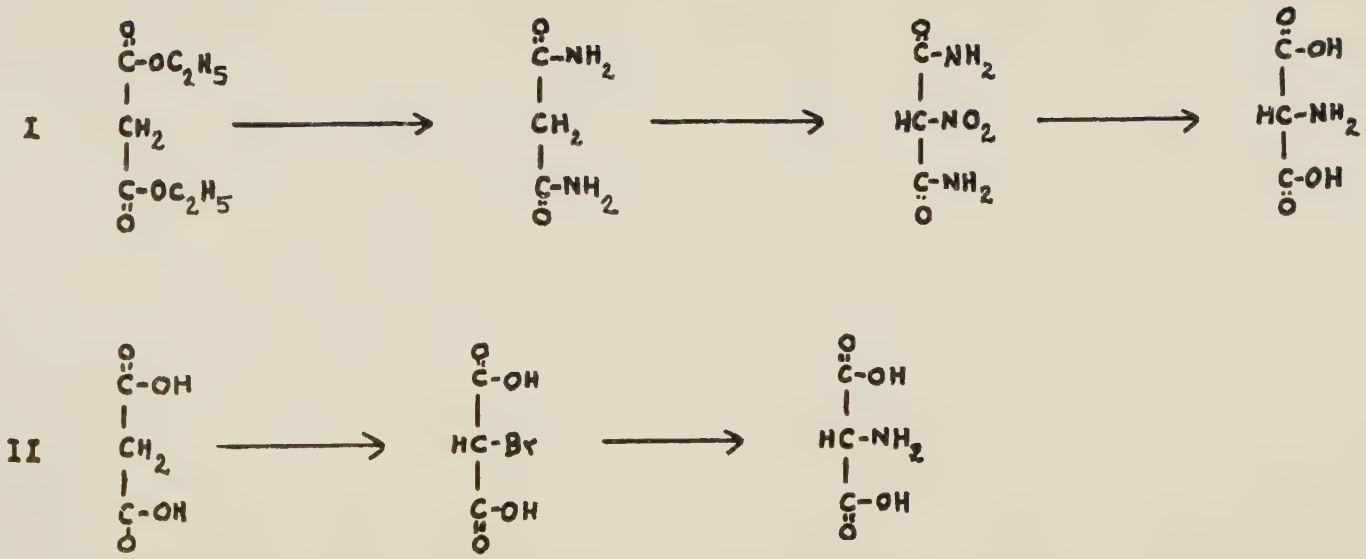

FIGURE 6

ate, the replacement of one ester group by an oxime group and subsequent simultaneous reduction of oxime and cyano groups to amines. The yield of cyanomethyldiethyl malonate was pitifully low, however, a side reaction occurring which completely obscured the desired material in tar, and the synthesis was abandoned.

Still another possible synthesis (Figure 4, scheme IV) involves the use of two phthalimide groups for introducing the two amino groups. Sörensen (12) prepared the higher homolog, α,δ-diaminovaleric acid by the same synthesis; but while he obtained the diphthalimido compound crystalline, apparently without difficulty, no method could be found to crystallize the diphthalimido compound of this synthesis, although many conditions of reaction and recrystallization were tried. A resinous material was obtained which had the correct percentage of nitrogen and was subjected to several methods of hydrolysis with rather inconclusive results. This work cannot be regarded as completed.

α, β-Diaminopropionic Acid

α,β-Diaminopropionic acid was prepared by Klebs (15) in 1904, and since then has received occasional study(16, 17, 18). It is usually synthesized by the method shown in Figure 5, sceme I, which was followed in this work, involving the preparation of ally alcohol from glycerol, the addition of bromine to the double bond of allyl alcohol, oxidation of the alcohol to dibrompropionic acid and conversion of the dibrom acid to diaminopropionic acid by means of ammonia under pressure. The overall yield is low and the final step is necessarily run in small amounts, but by numerous repetitions an adequate quantity of the hydrobromide of the acid was prepared.

As found by Neuberg and Ascher(19) when ammonium carbonate is included with ammonia and α, β-dibrompropionic acid in the final step of this synthesiss the chief product was found to be not α, β-diaminopropionic acid but isoserine, $CH_2(NH_2)CH(OH)COOH$. A number of experiments indicated that isoserine does not coordinate with cobalt; this was more or less expected as the complexes of α-hydroxy acids and of ethanolamine are not stable.

Aspartic Acid

Aspartic acid for preliminary experiments was obtained by the method of Dunn and Smart (20), as intermediates for the synthesis were on hand having been used in the synthesis of α,γ-diaminobutyric acid.This synthesis involves the condensation of ethyl chloracetate with sodium phthalimidodiethyl malonate (Figure 5, II) and subsequent hydrolysis of the condensation product. The directions of Dunn and Smart are wholly adtquate and their yield was checked accurately. For larger quantities the excelent method of Dunn and Fox(21) was followed (Figure 5, III).

Aminomalonic Acid

Aminomalonic acid has been prepared by the reduction of isonitroso malonic acid(22), by the reduction of nitromalonamide with sodium amalgam(23) and with aluminum amalgam(24) and by the reaction of brommalonic acid with ammonia in methyl alcohol (25).

The synthesis was attempted by the latter two methods, (Figure 6, I and II) which appeared to be most practical. While diethyl malonate can be converted in fair yield to malonamide, the conditions required for successful nitration were found to be so critical that the preparation of large amounts of pure material was very difficult. Reduction of nitromalonamide yielded only an oily preparation of aminomalonamide; this was hydrolyzed by barium hydroxide and barium aminomalonate obtained which had the correct barium content. Decomposition occurred during

the conversion of the barium salt to the free acid. Because of the poor yields this method was abandoned in favor of the synthesis through brommalonic acid.

The preparation of brommalonic acid is complicated by the reactivity of the methylene group of malonic acid. The hydrolysis of bromdiethyl malonate by the method of Biilmann and Madsen(26) even under the most closely controlled conditions leads to a large amount of by-product and gives a soapy brommalonic acid which is not very satisfactory.

Direct bromination of malonic acid was tried; only small amounts of pure product were obtained with considerable effort and sufficient quantities of aminomalonic acid were not obtained.

Formation of Tridentate Compounds

Strongly basic α,β,γ-triaminopropane was shown by Mann (5, 6) to dissolve cobaltic hydroxide and to expel ammonia from chloro-pentammino-cobalti chloride with the formation of the cobalt-triaminopropane complex. It was expected that the formation of the coordination compounds of the diamino acids and amino dicarboxylic acids would be somewhat more difficult because of their less pronounced basic or acidic character.

With the two acids obtained, however, α, β-diaminopropionic acid and aspartic acid, complex formation took place from both the oxide and pentammine although slowly; more rapid, however, is the reaction of the acids with carbonato-tetrammino-cobalti chloride with which the reaction is essentially complete.

Cobalt and α, β-Diaminopropionic Acid

By the action of α, β-diaminopropionic acid hydrobromide on cobaltic hydroxide a compound was obtained which had the correct cobalt and bromine content, had the equivalent conductance of a uniunivalent salt and is undoubtedly di(α, β-diaminopropionato)-cobalti bromide, $[Co(C_3H_7O_2N_2)_2]^+Br$.

The reaction of the hydrobromide and bromopentammino-cobalti bromide yields the same compound.

The action of α, β-diaminopropionic acid hydrobromide on carbonato-tetramino-cobalti chloride gave a mixture of equal amounts of the complex bromide and chloride as expected; one treatment of the mixture in solution with excess ammonium chloride increased the chloride to 70 per cent. No further attempt to convert the mixture to the chloride by ammonium chloride was made. An attempt to remove all of the halogen by means of freshly precipitated silver oxide failed due to the decomposition of the hydroxide of the complex.

A mixture of cobaltic sulfate* and α, β-diaminopropionic acid hydrobromide showed immediate reduction of the trivalent cobalt; whether the reduction occurred at the expense of the amino acid or the bromide, was not investigated as other successful methods of preparing the complex make this method superfluous.

Cobalt and Aspartic Acid

That aspartic acid and trivalent cobalt form a permanganate colored lake of some sort was briefly noted by Lifschitz(29).

The permanganate colored complex was now found to be formed by the action of aspartic acid on cobaltic oxide; but because of its extremely high solubility the material is inseparable from water by concentration. Evaporation to dryness resulted in the formation of a resin. Attempts

* Cobaltic sulfate was prepared by the anodic oxidation of a saturated solution of cobaltous sulfate in 10 N sulfuric acid (27, 28). Centrifuged green cobaltic sulfate still moist with sulfuric acid was used.

to precipitate the complex by the addition of ethyl alcohol, propyl alcohol, or acetone yield only oily emulsions. While boiling a solution with methyl cellosolve yields a granular solid, the product was not uniform and the cobalt content showed variations of 0.5 to 5 per cent.

The permanganate colored complex was also formed by reacting aspartic acid and carbonato-tetrammino-cobalti chloride, carbon dioxide and ammonia being given off. On the addition of methyl alcohol a flocculent lavender colored precipitate was thrown down. This material was filterable but even after several reprecipitations from water by methyl alcohol it appeared to be somewhat variable in composition. The filtered material when dried over calcium chloride forms a cake which is easily crushed. When dried over phosphorus pentoxidt in a vacuum at 100° this powdered material shows a reproducible loss in weight of 8.9 per cent. This corresponds almost exactly to one molecule of methyl alcohol of crystalization if the compound is assumed to be the ammonium salt of diaspartato cobalt, $[Co(C_4H_5O_4N)_2]NH_4$.

The compound is very stable towards acids but quite sensitive to alkali. Materials dried over phosphorus pentoxide was analyzed for cobalt by conversion to cobalt sulfate after decomposing with perchloric acid. The values for nitrogen, by the Kjeldahl method, were variable, due probably, to the difficulty of getting the sample completely decomposed; the addition of metallic selenium promoted the decomposition. The cobalt content averaged about one per cent above the theoretical value and the values for nitrogen obtained from the analyses in which selenium was used were 0.3 to 0.4 per cent high.

The equivalent conductance at infinite dilution was found by extrapolation of measured values to be about 95, the value of a uni-univalent salt. The negative character of the complex ion was shown by a migration experiment in agar gel; the permanganate color moved definitely toward the positive electrode.

The complex obtained by the action of aspartic acid on cobalt oxide and which, therefore, could not possibly contain any ammonia was also precipitated by methyl alcohol. The loss on drying over phosphorus pentoxide was much greater, and the material was much lighter in color. Analyses of the material however gave extremely variable results and as no checks were obtained none are reported. The conductivity of this preparation was appreciably higher than that of the material first mentioned. The substance is probably the free acid of the complex $H[Co(C_4H_5O_4N)_2]$.

The complex can also be prepared by the action of aspartic acid on bromo-pentammino-cobalt bromide if the mixture is made alkaline with ammonia.

There appears to be no oxidation of aspartic acid by cobaltic sulfate; if a mixture of the two is carefully neutralized with ammonia the permanganate colored complex forms immediately.

An attempt was made to prepare the sodium salt by treating a weighed amount of the ammonium salt with the calculated amount of 0.1 N sodium hydroxide. Decomposition with deposition of cobaltic oxide, occurred however.

EXPERIMENTAL DETAILS

Phthalimide

Phthalic anhydride was converted to phthalimide by tht methods of Organic Syntheses(32). Although the yield reported was obtained, a dfficulty was experienced in the first procedure which made the method troublesome. Reaction between phthalic anhydride (500 g.)and 28 per cent ammonium hydroxide (400 g.) occurs immediately; as the temperature is raised a cake of solid material suspended above the liquid is for-

med by sublimation and only a small amount of liquid is left boiling in the bottom of the flask, so that it is very difficult to get the entire mass fused.

More satisfactory is the fusion of phthalic anhydride with ammonium carbonate. For each 100 g. of anhydride 50 g. of ammonium carbonate was used (theoretical being 32.4 g.). Using a Rose burner and a large Pyrex round bottom flask, 5 kilograms of anhydride was converted at once. The reaction was carried out in a hood, the subliming excess carbonate and small amount of phthalimide simply allowed to escape. The clear, light yellow fusion was poured into galvanized pans, covered with paper and allowed to cool. The product melted at 221-223° and was converted directly to potassium phthalimide.

Potassium Phthalimide

The phthalimide prepared as described above was converted without recrystallization into the potassium salt using the method of Organic Syntheses(33). The yield was improved by cooling the alcohol-potassium phthalimide mixture to 0° to 5° with ice before filtering.

β-Bromethylphthalimide

β-Bromethylphthalimide was prepared from ethylene bromide and potassium phthalimide strictly according to the procedure of Organic Syntheses(34). M. p. 76-78° (uncorr.) Yields: 75 per cent.

Phthalimidoethyldiethyl malonate

Phthalimidoethyldiethyl malonate was fist prepared by the condensation of β-bromethylphthalimide and sodium diethyl malonate in alcohol solution by Aschan(8), who found its melting point to be 42-44°. Unable to obtain this compound as a crystalline material in good yield Fischer (7) employed a thick oily preparation in his synthesis of α, γ-diaminobutyric acid.

A number of condensations were run varying the conditions of the reaction with a view of improving the product. The use of alcohol freshly distilled from metallic calcium and well dried apparatus also resulted in an oily product; another condensation run in absolute alcohol prepared by Adiches' method(35),* and in apparatus dried at 215° overnight gave no better results. The β-bromethylphthalimide in these experiments was carefully dried in vacuum and the sodium, granulated under boiling toluene, was weighed under toluene. The condensation was run in the higher boiling ether-alcohol, methyl cellosolve, with no better results.

In general the procedure consisted in dissolving the sodium in alcohol, cooling, adding a slight excess of diethyl malonate, refluxing for 30 minutes and then adding slightly less than the theoretical amount of β-bromethylphthalimide. After refluxing 5 to 10 hours, the mixture was cooled, and steam distilled to remove alcohol and unchanged ester. The residual oily layer was then extracted with ether, heated for some time with Norite, filtered and evaporated to the point where a light brown oil began to separate. Scratching and cooling would not induce crystallization. A run in which the steam distillation was omitted, the alcohol removed under vacuum, the residue dissolved in water and benzene, the layers separated and the material then worked up, also gave an oil.

Recrystallization from a high boiling petroleum ether (previously purified by treatment with sulfuric acid and permanganate, washed with

* Fourteen g. of metallic sodium was dissolved in 2 l. of alcohol freshly distilled from lime and treated with 40 g. of ethyl fermate; after some refluxing the mixture was distilled, the first 300 c.c. being discarded, into apparatus dried at 215°.

caustic solution and water, dried and distilled) improved the color of the material but always yielded an oil.

These oily products when heated to 180° on a sand bath under vacuum of 0.5 mm. to remove all solvent were of variable nitrogen content and usually considerably below the theoretical.

The condensation was also attempted by a fusion between β-bromethylphthalimide and solid sodium diethyl malonate prepared in toluene. The oily product obtained from this reaction was high in nitrogen.

Towards the end of this work a further study(9) of this reaction appeared in which the condensation was carried out between the β-bromethylphthalimide and a suspension of sodium diethyl malonate in benzene; no crystallne product was obtained but the material was vacuum fractionated, boiling 225-235°/4.5 mm.

This work was promptly repeated, using toluene instead of benzene and employing mechanical stirring. A difficulty due to foaming and charring during the vacuum fractionation was solved by the use of a metal bath. The distillation was time consuming and the yield disappointingly small. The material obtained was used in the next step.

Phthalimidoethylbromdiethyl malonate

Phthalimidoethylbromdiethyl malonate was prepared by Fischer(7) by brominating oily phthalimidoethyldiethyl malonate in chloroform in sunlight. After two to three days he removed the excess bromine with sulfite, evaporated away the chloroform and recrystallized by dissolving the residue in hot alcohol, and cooling to —20°. Colorless crystals were obtained melting at 76-78°.

This work was repeated exactly. Only a small amount of very oily crystals was obtained after two recrystallizations and these melted between 170° and 190°. Repetitions of this process, in pyrex and in quartz with exposures up to a month in sunlight yielded non-crystallizing oils. Phthalimidoethyldiethyl malonate vacuum distilled was brominated in this same manner but yielded only an oily product.

In another attempt the oil was dissolved in chloroform and the exact amount of bromine added to the gently refluxing solution. The reaction was worked up as above. Oily material resulted.

An attempt to distill some of this oily material was abandoned due to severe foaming.

The oils obtained from some of these brominations were used in the next reaction which consisted in hydrolyzing the ester with hydrobromic acid saturated with hydrogen bromide at 0°, and the product from this was decarboxylated by heating at 140°-150°.

Small amounts of solids were obtained but their melting points varied widely and were far from the values reported by Fischer.

This work was very inconclusive. The indefiniteness of the results and the uncertain nature of the compounds involved make this entire synthesis unsatisfactory.

Ethyl chloracetate

Chloracetic acid was esterified by the method of Conrad(36, 20). A mixture of 200 g. of chloracetic acid, 130 c.c. absolute ethyl alcohol and 25 g. of sulfuric acid was refluxed for several hours. The ester layer was separated, washed with water, then with bicarbonate solution, and finally with water. The ester was dried over anhydrous sodium sulfate and then distilled. The yield of ester boiling at 136-140°/745 mm. was 198 g. corresponding to 76.5 per cent.

Chloracetamide

Ethyl chloracetate was converted to chloracetamide by treatment with

aqueous ammonia(37). One volume of ester and two volumes of concentrated ammonium hydroxide were shaken together in a separatory funnel held under running water. After 15 minutes the beautiful snow white crystals were filtered off, washed with mother liquor and with a little ice cold water. The yields were almost quantitative; m. p. 113-114°.

Chloracetonitrile

Chloracetamide was dehydrated to chloracetonitrile by phosphorus pentoxide as described by Steinkopf(38). Into a well dried flask through which was passed a slow stream of dry air was introduced 50 g. of chloracetamide and then 80 g. of phosphorus pentoxide; the solids were then thoroughly mixed by shaking. Partial vacuum was then applied and the mixture gently heated. Heating was continued as long as liquid distilled over, good vacuum being applied toward the end of the reaction. The liquid obtained was then distilled over phosphorus pentoxide. Yield: 26.5 g. (70 per cent) boiling at 123°/746 mm.

Cyanomethyldiethyl malonate

To 12.5 g. of metallic sodium dissolved in absolute alcohol was added 80 g. of diethyl malonate. After refluxng for 30 minutes, 39 g. of chloracetonitrile was added slowly. Vigorous reaction occurred instantly, the solution becoming green and finally chocolate brown. After four hours' refluxing the mixture was steam disitlled and the insoluble red material extracted with ether. The ether extract was dried over anhydrous magnesium sulfate. After filtering off the magnesium sulfate, the ether was removed and the residue distilled in vacuum. The liquid boiled over a wide range and a very large amount of solid residue was left. The fraction boilng from 100 to 200° was collected and redistilled yielding 7.5 g. of clear liquid boiling fairly constantly at 155-165°/18 mm.

A variation of the method of working up the reaction mixture was tried. Instead of steam distilling, the alcohol was removed by vacuum distillation, and the residue was treated with water. The oily layer was then extracted with ether. After removal of the ether the liquid was vacuum distilled. Foaming and decomposition occurred and the run was abandoned.

Hydrolysis of cyanomethyldiethyl malonate

The cyanomethyldiethyl malonate obtained above was treated with 10 g. of sodium hydroxide dissolved in 15 c.c. of water. A white solid separated immediately on mixing but quickly disolved. The solution was heated on the steam bath for six hours after which ammonia evolution had ceased. The solution was cooled, mixed with ice and neutralized with sulfuric acid. The solution was then filtered and evaporated to a volume of 60 c.c. The solution was then extracted with ether. On treating the ether extract with petroleum ether an oil separated which quickly solidified. This material when recrystallized from ether melted at 171-174°; reported for α,α,β-ethane tricarboxylic acid, the expected hydrolysis product, 159°. α,α,β-Ethane tricarboxylic acid was obtained by alkaline hydrolysis of the triethyl ester obtained by condensing ethylchloracetate with malonic ester. This acid is fairly readily decomposed and unless care was taken in the recrystallization, some succinic acid was formed and the melting point raised 10 to 15 degrees as observed with the material obtained from the hydrolysis of cyanomethyldiethyl malonate.

Diethyl brommalonate

Diethyl malonate was brominated in carbon tetrachloride solution as described in Organic Syntheses(39). It was found that mechanical stirr-

ing was not necessary if the solution was kept refluxing well during the bromine addition. Yield: 86 per cent, b. p. 122-128°/20 mm.

Phthalimidodiethyl malonate

Potassium phthalimide and diethyl brommalonate were coupled as described in Organic Syntheses(40). Best results were obtained when the potassium phthalimide had been dried overnight at 110° and when the ethyl brommalonate was freshly distilled. Even then it was frequently necessary to heat the mixture as high as 150° to initiate the reaction. The reaction mixtures were worked up as described and the yields were uniformly good.

Sodium phthalimidodiethyl malonate(41)

Conversion of phthalimidodiethyl malonate to sodium phthalimidodiethyl malonate by sodium ethylate was found very unsatisfactory; the pasty mass which results cannot be filtered and removal of the alcohol in vacuum is practically impossible. A procedure similar to that of Dunn and Smart(20) was finally adopted. Fifteen grams freshly cut metallic sodium, 200 g. of phthalimidodiethyl malonate and 300 c.c. of toluene were mixed in a 1-liter two-neck, round botton flask, fitted with a mechanical stirrer (through mercury seal) and a reflux condenser. The mixture was refluxed and vigorously stirred for three hours. After cooling, the mixture was filtered and washed with toluene. The light yellow solid was then dried at 110° in a vacuum.

Phthalimidoethylphthalimidodiethyl malonate

The condensation of β-bromethylphthalimide and phthalimidodiethyl malonate was attempted under a variety of conditions. In no case was a crystalline product obtained but from the fusion at 200°, using sodium phthalimidodiethyl malonate prepared as described above, was obtained a thermo-plastic resinous material which had the correct percentage of nitrogen (Kjeldahl) and which was used in the subsequent reaction.

Condensations were run in absolute ethyl alcohol, methyl cellosolve, butyl cellosolve, and carbitol. In general the procedure involved dissolving sodium in the freshly distilled alcohol or alcohol-ether, adding the phthalimidodiethyl malonate, refluxing for one hour, adding the β-bromethylphthalimide and finally refluxing for 20 hours. The reaction mixture was worked up by steam distillation, extraction of the oily residue with ether, digestion for some time with Norite, and evaporation of the ether from the filtrate. In case of the high boiling carbitol (190-200°), decomposition occurred; in the others a light yellow oily product was obtained which could not be crystallized. While soluble in petroleum ether (150-170°), evaporation and cooling always yields a non-crystallizing oil. The addition of finely divided copper to the condensation mixture did not appear to aid the reaction. Hydrolysis of these oils with concentrated hydrochloric acid yielded phthalic acid but no diamino acid. The oily products obtained by these methods were always low in nitrogen (Kjeldahl):

Calculated for $C_{25}H_{22}O_8N_2$: N = 5.858%

Found: N = 4.78%, 4.89%, 4.87%

In the fusion method 100.0 g. of sodium phthalimidodiethyl malonate, dried at 100° in a vacuum, and 77.7 g. bromethylphthalimide were heated together at 200-222° for five hours on a oil bath. After cooling, the mixture was extracted with hot benzene and water. The benzene layer was refluxed with Norite for a few hours, filtered and the benzene removed by distillation; good vacuum was applied at the end to insure

the removal of all solvent. The dark resinous residue was analyzed for nitrogen by the Kjeldahl method:

Calculated for $C_{25}H_{22}O_8N_2$: N = 5.858%
Found: N = 5.88%, 5.90%

Hydrolysis of phthalimidoethylphthalimidodiethyl malonate

A. Several attempts were made to convert the phthalimidoethylphthalimidodiethyl malonate directly to diaminobutyric acid, that is, to split off the phthalic acid residues, hydrolyze the ester groups and decarboxlate simultaneously. Gabriel(13) was able to convert the much simpler phthalimidopropyldiethyl malonate directly to δ-aminovaleric acid in one step by concentrated hydrochloric acid at 180-190°; and Aschan(14) similarly prepared γ-aminobutyric acid by heating phthalimidoethyldiethyl malonate with concentrated hydrochloric acid to 170-180° for three hours.

The reactions were carried out in an open test tube in a brass bomb. A mixture of 15 g. of ester and 70 c.c. of concentrated hydrochloric acid was heated to 200° for 4 hours. Gas escaped on opening the cooled bomb; about the theoretical amount of insoluble phthalic acid was recovered and the hydrochloric acid filtrate yielded dark oily crystalline material on evaporation. This material, however, gave no precipitate with oxalic acid while Fischer reported α, γ-diaminobutyric oxalate insoluble. Attempts to convert the material to the benzoyl derivative failed.

B. The same total hydrolysis as described under A was applied successfully by Dunn and Smart(20) to the conversion of ethane-α-phthalimido-α,α,β-tricarboxylic acid triethyl ester to aspartic acid, using as reagent a mixture of 450 c.c. of ethyl alcohol and 250 c.c. of concentrated hydrochloric acid per 50 g. of material.

The thick oily phthalimidoethylphthalimidodiethyl malonate was refluxed with a mixture of alcohol and hydrochloric acid in the above proportions; the carbon dioxide evolved was collected in sodium hydroxide solution in a ten bulb tube and determined as barium carbonate. In several runs lasting 24 hours only a fraction of the theoretical amount of CO_2 was collected; and the amounts of insoluble phthalic acid recovered after removal of solvent were also variable and far below the theoretical. While one run gave a crystalline material, having a nitrogen content of 11.7 per cent, the products for the most part were oily. It appeared that a number of things were happening, all more or less completely. The crystalline material isolated was probably a compound in which one phthalic acid group was still retained.

C. An attempt was made to saponify the ester groups without splitting off the phthalic acid residue by the method used by King, L'Ecuyer and Openshaw(9) for hydrolyzing phthalimidoethyldiethyl malonate.

A mixture of fifty g. of resinous phthalimidoethylphthimidodiethyl malonate and 300 c.c. of acetic anydride was treated carefully with 500 c.c. concentrated hydrochloric acid. The mixture was boiled exactly 50 minutes in an open flask. The solvent was then removed under vacuum. The residual somewhat crystalline material was dissolved in sodium hydroxide solution and filtered from tarry insoluble material. The filtrate was acidified with hydrochloric acid. No immediate separation occurred but on standing overnight light brown solid separated; on longer standing more solid separated. This solid was filtered off, and dissolved in alcohol; cooling gave no precipitate but on evaporating a light yellow scale appeared. When dried, it melted sharply at 186-188° with decomposition.

Two repetitions of this reaction on the same material under apparently the same conditions yielded large amounts of hopeless tars and practically no crystalline material.

Allyl alcohol

The method of Organic Synthesis(42) was used, based on the reaction of glycerol with formic acid and the subsequent decomposition of the glyceryl formate produced. Due to the large amounts of unbearable gaseous decomposition products eliminated, the set-up had to be modified by the inclusion of an efficient condenser in the form of a glass spiral surrounded by a salt and ice mixture. The 45-46 per cent yield reported in Organic Syntheses is based on repeated treatment of the glycerol by formic acid; since the price of formic acid is about three times that of glycerol at the present time it is more economical to use up the formic acid at the expense of the glycerol. The alcohol-water mixtures obtained were analyzed by bromine titration (standardized against As_2O_3). Yield based on glycerol: 12.5 per cent.

β, γ-Dibrompropyl alcohol

The allyl alcohol-water mixtures obtained above were combined with an equal volume of carbon disulfide, cooled in salt and ice, and with vigorous stirring treated carefully with the required amount of bromine mixed with an equal volume of carbon disulfide. The lower layer consisting of carbon disulfide and brominated alcohol was then separated from the water, and the carbon disulfide expelled on the steam bath. The alcohol was then fractionated under reduced pressure. A yield of 90 per cent was obtained of β, γ-dibrompropyl alcohol boiling at 120°/20 mm. A few cubic centimeters was collected boiling up to 128°.

α, β-Dibrompropionc acid

β, γ-Dibrompropyl alcohol was oxidized to α, β-dibrompropionic acid by the method of Kohler(43). A cold mixture of 246 c.c. of concentrated nitric acid and 88.6 c.c. of fuming nitric acid was added to 250 g. of cold dibrompropyl alcohol. The mixture was surrounded by salt and ice. A moderate reaction occurred, abundant amounts of oxides of nitrogen being evolved. On standing a few days a dark oil separated. Without separation the mixture was evaporated in a porcelain evaporating dish on the steam bath to expel the nitric acid and water. The residual oil was transferred to a fractionating flask. Some further water distilled off and around 130° a short evolution of colored gases occurred; the acid then distilled at a constant temperature. From eight such runs, using 2000 g. of alcohol, 1640 g. of dibrom acid were obtained corresponding to 77 per cent of the theoretical yield. The boiling points recorded were 130-135°/12-15 mm., 147°/20 mm., 156°/38 mm. On cooling the acid solidified to a crystalline mass. The material melted at 45-50°; reported: 51° (unstable form). After having stood over $CaCl_2$ in a desiccator for several months the material melted at 62-64°; reported for stable form, 64°.

α, β-Diaminopropionic acid hydrobromide (15,16,17.18,19)

α, β-Dibrompropionic acid was converted to diaminopropionic acid by means of ammonia under pressure. Concentrated ammonium hydroxide was saturated at 0° with ammonia gas, the density of the ammonia finally used beng 0.872. Thirty grams of α, β-dibrompropionic acid, previously treated with a small amount of ammonia and cooled, was mixed with 200 c.c. of saturated ammonia and the mixture was heated in a open glass tube in a steel pressure vessel to a temperature of 120°, at apressure of about 150 lbs. After 4 to 5 hours the vessel was cooled, the mixture was transferred to an evaporating dish and the ammonia expelled by heating on the steam bath. The dark residue was taken up with a little hot water, the solution evaporated somewhat, cooled and the solid material filtered off. This impure hydrobromide weighed 12 to 15 g. It was dissolved in hot water, heated for some time with Norite, filtered and

treated with 2 to 3 volumes of alcohol. After standing for some time, the precipitate was filtered off, washed with alcohol and dried. Yield: 4 g., 30 per cent; melting point: 226-230°, reported 228-230°, 238°.

Calculated for: $C_3H_8O_2H_2 \cdot HBr$: 43.21% Br
Found: 42.95% Br

Ethane-α-phthalimido-α,α,β-tricarboxylic acid triethyl ester(20)

Fifty g. of sodium phthalimidodiethyl malonate and 112 g. of ethyl chloracetate were refluxed for 2 to 2.5 hours on an oil bath. The ethyl chloracetate was removed by vacuum distillation. The residue was treated with water and ether and the layers separated. The ether was removed by distillation on the steam bath. To insure removal of all solvent the mixture was finally heated to 150° on a sand bath with the application of a good vacuum (oil pump). The residual oil was analyzed for nitrogen by the Kjeldahl method.

Calculated for $C_9H_{21}O_8N$: N = 3.58%
Found: N = 3.69%

Aspartic Acid(20)

The oil obtained above (51 g.) was treated with 450 c.c. of ethyl alcohol, 250 c.c. of concentrated hydrochloric acid and the mixture was refluxed 30 hours. The liquid was then evaporated under vacuum on the steam bath. The brown oil-solid residue was digested with 50 c.c. of water and the insoluble phthalic acid filtered off. The filtrate was heated for a few hours with Norite, and filtered. The well washed freshly precipitated silver oxide from 23 g. of silver nitrate was added and after short digestion, the precipitate of silver chloride was filtered off. Sufficient dilute hydrochloric acid was added to the filtrate to precipitate dissolved silver and after some heating the solution was cooled and filtered. The filtrate was evaporated to 100 c.c. An equal volume of alcohol was added and the mixture allowed to stand in the ice box. After two days 6 g. of white crystals were obtained which after drying turned brown at 280° and decomposed at 315°. Reported decomposition point 311-326°.

Ethyl fumarate

Eastman's technical fumaric acid was esterified by the method of Corson, Adams and Scott(44). Their apparatus was modified by the introduction of a 36 inch fractionating column packed with beads. This gave a more efficient separation of ester and water and improved the yields to 90-92 per cent.

Diketopiperazine diacetamide(21)

Ethyl fumarate was converted to diketopiperazine diacetamide by alcoholic ammonia under pressure. The reactions were carried out in ginger-ale bottles which were tested with 25 per cent aqueous ammonia at 100°. Rubber stoppers were well wired down and the bottles were well wrapped in cloth to minimize the danger of flying glass in case of explosion.

Eighty-two grams of ammonia gas were dissolved in 1100 c.c. of absolute alcohol at 0°; this was mixed with 172 g. of ethyl fumarate and the mixture divided among five bottles. These were then maintained at 100° for 24 hours in a boiling water bath. After cooling the alcoholic ammonia was removed by vacuum on the steam bath and the light brown solid obtained was used directly in the next step.

Copper Aspartate(21)

The crude diketopiperazine diacetamide was refluxed 6 hours on an

oil bath with strong sodium hydroxide; the resulting solution was made acid to methyl red with hydrochloric acid and then added to a hot solution of 220 g. of copper acetate. On short heating and standing for 10 hours an abundant yield of light blue copper aspartate was obtained.

Aspartic Acid(21)

Copper aspartate was suspended in 2 percent acetic acid and the cooper precipitated with hydrogen sulfide. When precipitation was complete the solution was boiled for 30 minutes and filtered. The filtrate was evaporated to half its volume under vacuum and treated with an equal volume of 95 per cent alcohol. After standing the fine white crystals of aspartic acid were filtered off. This material was used without further purification.

Calculated for $C_4H_7O_4N$: N = 10.53%
Found: N = 10.98%, 10.87%

Malonamide

Malonamide was prepared from diethyl malonate and concentrated ammonium hydroxide by the method of Freund(45). The yields averaged about 55 per cent of the theoretical.

Nitromalonamide

Malonamide was nitrated in fuming nitric acid following a procedure described by Johnson and Nicolet(24). If the temperature was allowed to rise above 10° no nitration occurred; below 0° no reaction took place. The reaction was controlled by the addition of solid carbon dioxide whenever the temperature threatened to rise. The yields from this reaction were highly variable but were usually very poor. The material used melted at 172°; reported, 172°.

Aminomalonamide and barium aminomalonate

The aluminum amalgam prepared from 20 g. of granulated aluminum was added to 25 g. of nitromalonamide and 75 c.c. of 10 per cent ammonia. Vigorous reaction occurred and the material became dry. After some time the mixture was extracted with 250 c.c. of boiling water and the filtered extract evaporated under vacuum. Reddish brown oily material separated which did not solidify on recrystallization from alcohol.

The oily material was hydrolyzed directly by refluxing for 10 hours with 54 g. $Ba(OH)_2 \cdot 8H_2O$ in 500 c.c. water. The precipitate was filtered off and digested with hot water, in which it appeared to be almost completely insoluble. Yield: 23 g., 53.5 per cent based on nitromalonamide. The material was dried at 110° and analyzed.

Calculated for BaC_3O_4N: Ba = 53.99%
Found: Ba = 53.77%, 53.79%

Aminomalonic acid

The barium salt obtained above was suspended in 300 c.c. of water and treated with the calculated amount of normal sulfuric acid. The mixture was left on the hot plate overnight. Insoluble barium sulfate was filtered off and the solution evaporated in a vacuum and finally over calcium chloride. Yellow brown material remained which melted above 150°; reported for aminomalonic acid, 109°. Decomposition of the acid probably occurred during the overnight digestion. No further attempt was made to prepare the acid by this method.

Brommalonic acid

A. Bromdiethyl malonate was hydrolyzed by the method of Bülmann and Madsen(26); the conditions given were observed very carefully. From a run starting with 100 g. of bromdiethyl malonate, 12 g. of by-product (ethane tetracarboxylic acid tetraethyl ester) were obtained and

13 g. (39 per cent) of lard-like brommalonic acid, which could not be recrystallized from benzene, acetone, or chloroform. The conditions of this reaction are very critical, the procedure is time consuming, and the product rather unsatisfactory.

B. The direct bromination of malonic acid is complicated by the formation of dibrommalonic acid, and brominated acetic acids(25). The ether bromination method of Conrad and Reinbach(30) as modified by West (31) was followed. The removal of hydrobromic acid by washing with water seriously decreased the yield; the limitation to small quantities and the time consumed in long evaporations over caustic make the method impractical for the preparation of reasonable amounts of the acid.

Bromination was attempted in carbon disulfide but only a very small quantity of brommalonic acid was obtained on recrystallization from acetone and benzene.

Bromo-pentammino-cobalti-bromide

Bromo-pentammino-cobalti bromide was first prepared by the air oxidation of an ammoniacal solution of cobalt bromide(46) and has also been obtained from aquo-pentammino-cobalti oxalate(47) and from aquo-pentammino-cobalti hydroxide(48). The latter methods are indirect and the yield in the air oxidation is very poor. Oxidation by hydrogen peroxide was suggested by the method of Willard and Hall(49) for the preparation of the analogous compound chloro-pentammino-cobalti chloride; it was also found to work excellently for bromo-pentammino-cobalti bromide. In order to establish the optimum conditions, three series of runs were made varying the quantities of ammonium bromide, of ammonia and of hydrogen peroxide. The amounts cannot be decreased below the quantities given without seriously affecting the yield.

Twenty-five g. (0.21 mole) of cobalt carbonate* was treated carefully with 65 c.c. of 42 per cent hydrobromic acid. The solution was filtered by suction through a fritted glass filter to remove any undissolved oxide possibly present. The filtrate in a 1-L. beaker was treated with 50 g. (0.51 mole) of ammonium bromide and then 250 c.c. of concentrated ammonium hydroxide (approximately 3.5 mole NH_3) Disregarding the pink precipitate which appeared, 40 c.c. of 30 per cent hyrogen peroxide (0.39 mole) was added slowly with stirring. When the vigorous efferescence had ceased the oxidation was complete and the solution dark red in color. While still warm the solution was placed in the hood and a vigorous stream of air blown through for two or three hours to remove excess ammonia. The solution was then neutralized with hydrobromic acid until the rose colored precipitate*, forming as the solution became neutral, persisted and then an excess of 50 c.c. of the acid was added. The entire precipitate and solution were transferred to an evaporating dish and heated on the steam bath for two hours. The precipitate was filtered on a Buchner funnel, washed by mixing with 230 c.c. of water and again filtered. The product was then washed with four 25 c.c. por-

* Cobalt carbonate was prepared by the addition of sodium bicarbonate solution to a boiling solution of cobalt chloride, washing by repeated suspension in water and refiltering until chloride free and drying in a vacuum at 110°; four samples so prepared analyzed: 51.9, 44.1, 53.9, 53.8% Co; theoretical: 49.55% Co.

* This rose colored precipitate is aquo-pentammino-cobalti bromide; it can be filtered at this point and the aquo salt remaining in solution recovered by the addition of an equal volume of 95% alcohol. In this way 75 g. (82% of the theoretical) of material, dried over sulfuric acid, can be obtained.

	Co	Br	NH_3	H_2O
Calculated for $[Co(NH_3)_5H_2O]Br$:	14.67	59.66	21.19	4.48
Found:	14.82	59.84	21.15	4.43
	14.84	59.55	21.17	

tions of alcohol and dried at 110°. The product was finely cryrtalline, light lavender in color and weighed 70 to 75 g., about 90 per cent of the theoretical yield based on the cobalt content or the cobalt carbonate used.

The product was recrystallized by the gradual addition of 25 g. of the material to a mixture prepared by adding 25 c.c. of ammonium hydroxide to 500 c.c. of water heated to 90° .The solution was filtered, 40 c.c. of hydrobromic acid was added, and the whole was heated on the steam bath for two hours. The large purple crystals were filtered, washed with water and alcohol and dried. Recrystallization was found to make little difference on the analysis of the material, so that the unrecrystallized material was used in further work.

	Co	Br	NH_3
Calculated for $[Co(NH_3)_5Br]Br_2$:	13.36	62.46	22.18
Found*			
1st product:	15.45	62.69	22.24
	15.52	62.55	22.08
		62.54	
recry. product:	15.43	62.42	22.04
	15.43	62.28	22.05
		62.34	

Carbonato-tetrammino-cobalti chloride

Carbonato-tetrammino-cobalti chloride was prepared by Jörgensen(50) by the air oxidation of a mixture of cobalt chloride, ammonia, and ammonium carbonate. The use of hydrogen peroxide as an oxidizing agent for this reaction was found to be satisfactory and to effect a considerable saving in time.

Forty grams of $CoCl_2 \cdot 6H_2O$ were dissolved in 100 c.c. of water, and then 400 g. of ammonium carbonate and 1000 c.c. of concentrated ammonia were added. Twenty-five c.c. of 30 per cent, hydrogen peroxide was then added carefully with stirring; vigorous effervescence occurred and oxidation appeared to be complete immediately. The mixture was evaporated on the steam bath, with occasional addition of ammonium carbonate, to about 200 c.c. The solution was cooled in ice and then 1500 c.c. of alcohol was added slowly with stirring. The dark rose colored product was filtered and air dried. Yield: 32 g., 85 per cent. If too suddenly thrown out of solution the product is somtimes oily, but becomes crystalline on standing.

Di(α,β-diaminopropionato)-cobalti bromide

A. To 2.18 g. of $CoCl_2 \cdot 6H_2O$ dissolved in 200 c.c. of boiling water was added a few c.c. of 30 per cent hydrogen peroxide; sodium hydroxide solution was then added dropwise in slight excess. After the vigorous reaction was over the precipitate of cobaltic hydroxide was digested for several minutes and then washed alkali free with centrifugal drainage. The moist hydroxide was then suspended in a solution of 3.38 g. of α, β-diaminopropionic acid hydrobromide and heated on the steam bath. After 20 hours heating the solution was filtered from a little unreacted oxide and evaporated to 10 c.c. On cooling a light rose solid separated which was filtered off and recrystallized from hot water.

* The material was analyzed as follows: the cobalt was determined by heating a sample in a porcelain crucible with sulfuric acid, igniting finally at 550° and weighing as cobalt sulfate; the bromine was determined as silver bromide by precipitation from either (1) a solution in which the complex had been decomposed by boiling with hydrazine hydrate, or, (2) from a boiling solution slightly acid with nitric acid; the ammonia was determined by Kjeldahl distillation.

Material dried over phosphorus pentoxide in a vacuum at 100° was analyzed.

		Co	Br
Calculated for $[Co(C_3H_7O_2N_2)_2]Br$ mol. wt.: 345.1		17.08	23.16
	Found:	16.94	23.16
		16.97	23.45

Equivalent conductance = 102.1 for 0.001 M solution.

B. To 2.1 g. of bromo-pentammino-cobalti bromide suspended in 200 c.c. of water was added a solution of 2.0 g. of α, β-diaminopropionic acid hydrobromide. The solution was boiled gently for two hours and then the volume reduced by evaporation. On cooling and filtering there was obtained a crystalline material identical in color and properties with the bromide described above.

Di(α,β-diaminopropionato)-cobalti chloride

Solutions of 3.70 g. of α, β-diaminopropionic acid hydrobromic and 2.32 g. of carbonato-tetrammino-cobalti chloride in water were mixed and heated gently for two hours. Carbon dioxide and ammonia were evolved. The solution was concentrated and cooled. A rose colored solid was obtained which was dissolved in hot water and treated with ammonium chloride. An equal volume of alcohol was added, the solid thrown down was filtered off and again recrystallized from hot water. This material was dried over phosphorus pentoxide and analyzed for cobalt and chloride. The chloride content was higher than the theoretical, the cobalt lower; indirect calculation based on both analyses indicated the material to consist of about 70 per cent chloride, 30 percent bromide. No further attempt was made to convert more of the complex to the chloride by ammonium chloride.

The preparation was repeated and the mixture of salts in solution in water was treated with a hot suspension of the calculated amount of alkali free silver hydroxide, the object in view being the removal of all halogen. The hydroxide of the complex base was not stable in hot water, however, for decomposition occurred, and the reaction was abandoned.

Cobalt complex with aspartic acid

A. To 4.4 g. of carbonato-tetrammino-cobalti chloride in 150 c.c. of water was added 5.2 g. of aspartic acid in 150 c.c. of water. The mixture was heated gently for about five hours until the evolution of carbon dioxide and ammonia appeared complete and the solution had assumed a deep permanganate color. The solution was then concentrated under vacuum on the steam bath to a volume of 50 c.c., cooled and filtered to remove traces of cobalt oxide. Several volumes of methyl alcohol were then added to the solution. A flocculent lavender precipitate of the complex appeared and was filtered off. The material was immediately put into a desiccator over calcium chloride. Yield: 2.6 g., 39 per cent of the theoretical. The filtrate was again concentrated and again treated with methyl alcohol yielding a second crop of 0.5 g. Still more material can be recovered by a repetition of this process. The combined precipitates were then dissolved in water and reprecipitated by the addition of methyl alcohol. The precipitates were dried over phosphorus pentoxide at 100°, and the losses in weight recorded.

0.8420 g. lost 0.0746 g. or 8.86 per cent
1.0758 g. lost 0.0970 g. or 9.01 per cent

Assuming the compound to be $[Co(C_4H_5O_4N)_2]NH_4$ this loss corresponds to 1.03 and 1.05 molecules of methyl alcohol of crystallization.

		Co	N	
Calculated for $[Co(C_4H_5O_4N)_2]NH_4$		17.38	12.39	
Found	(as $CoSO_4$)	18.43	15.32	
		18.35	12.67	
		18.82	14.67	
		18.42	14.42	
		18.39	12.67	(Se)
	(as Co_3O_4	18.68	12.46	(Se)
			12.98	(Se)

Equivalent conductance

Conc.		
0.001	87.9	
0.0005	91.3	
0.00025	92.3	
0.0001	93.6	
0.0000	95	(by extrapolation)

The sign of the charge on the complex was determined by a migration experiment. In the bottom of a U-tube was placed an agar gel (10 g. agar in 500 c.c. boiling water) containing some of the complex salt. A little carbon was placed on this on each side of the boundary, then layers of clear agar containing potassium chloride, finally saturated potassium chloride solution. The U-tube was then placed in a freezing mixture and 0.05 amp. was allowed to pass for 3 hours using platinum electrodes. There was a distinct movement of color toward the positive electrode showing the complex to be negative in character.

B. To a suspension of 3.83 g. of bromo-pentammino-cobalti bromide in 200 c.c. of water was added a solution of 2.66 g. of aspartic acid. After some heating everything dissolved and the solution was cherry red in color, but of distinctly digerent color than the expected complex. On adding ammonia and heating for some time further the solution assumed the permanganate color of the complex. After the solution had been evporated somewhat the material was recovered by the addition of methyl alcohol as above. Yield 2.45 g., about 72 per cent.

C. Cobaltic hydroxide prepared from 2.38 of $CoCl_2 \cdot 6H_2O$ was treated with 2.66 g. of aspartic acid in 200 c.c. of water. The mixture was heated for 20 hours with occasional replacement of water. A small amount of undissolved hydroxide was filtered off, the permanganate colored solution concentrated somewhat and methyl alcohol added. A precipitate, like the ones obtained above, was obtained. The material was dissolved in water and reprecipitated by the addition of methyl alcohol. Dried over phosphorus pentoxide, the material was lighter in shade than the ammonium salt. Analysis of the material gave erratic results. The equivalent conductance of a 0.0001 M solution was 147, appreciably higher than the value obtained for the ammonium salt above. The compound is probably the free acid $H[Co(C_4H_5O_4N)_2]$.

SUMMARY

1. Gaps in the field of the coordination compounds have been pointed out and an attempt has been made to prepare compounds shown by models to be theoretically possible between metals and organic molecules bearing three associating groups.

2. Compounds between cobalt and α, β-diaminopropionic and aspartic acid have been isolated. Analytical data and chemical behavior indicate that the compounds are di(α,β-diaminopropionato)-cobalti bromide, $[Co(C_3H_7O_2N_2)_2]Br$, and ammonium diaspartato-cobaltiate $NH_4[Co(C_4H_5O_2N)_2]$, in which one organic molecule occupies three of the coordination positions about the metal atom, that is functions as a tridentate group.

3. Difficulties with the Fischer synthesis of α,β-diaminobutyric acid have not been overcome and new methods tried have not been successful.

4. Peroxide oxidation was shown to improve the syntheses of the cobalt-ammines, bromo-pentammino-cobalti bromide and carbonato-tetraammino-cobalti chloride.

BIBLIOGRAPHY

1. Morgan and Drew, J. Chem. Soc. **117**, 1457 (1920)
2. Morgan and Smith, J. Chem. Soc. **127**, 2030 (1925)
3. Sidgwick, "The Electronic Theory of Valency", Oxford University Press, London, 1929, p. 233
4. Pfeiffer, Ann **503**, 84 (1933)
5. Pope and Mann, Proc. Royal Soc. **107**, 80 (1925)
6. Mann, J. Chem. Soc (1926) 2681
7. Fischer, Ber. **34**, 2900 (1901)
8. Aschan, Ber. **24**, 2449 (1891)
9. King, L'Ecuyer, and Openshaw, J. Chem. Soc. (1936) 353
10. Crawford and Kenyon, J. Chem. Soc (1927) 397
11. Fischer and Weigert, Ber. **35**, 3772 (1902)
12. Sörensen, Chem. Zentr. (1903) II, 33
13. Gabriel, Ber. **23**, 1767 (1890)
14. Aschan, Ber. **24**, 2449 (1891)
15. Klebs, Z. physiol. Chem. **19**, 322 (1894)
16. Winterstein and Küng, Z. physiol. Chem. **59**, 144 (1909)
17. Neuberg and Silbermann, Ber. **37**, 342, (1904)
18. Frankland, J. Chem. Soc. **97**, 1318 (1910)
19. Neuberg and Ascher, Biochem, Z. **6**, 559 (1907)
20. Dunn and Smart, J. Biol. Chem. **89**, 47 (1930)
21. Dunn and Fox, J. Biol. Chem. **101**, 494 (1933)
22. Baeyer, Ann. **131**, 295 (1864)
23. Ruheman and Orton, J. Chem. Soc. **67**, 1007 (1895)
24. Johnson and Nicolet, J. Amer. Chem. Soc. **36**, 361 (1914)
25. Lutz, Ber. **35**, 2549 (1902)
26. Biilmann and Madsen, Ann. **402**, 341 (1914)
27. Müller, "Laboratory Manual of Electrochemistry", Routledge, London, 1931, Experiment 55
28. Swann and Xanthakos, J. Amer. Chem. Soc. **53**, 400 (1931)
29. Lifschitz, Z. phy. Chem. **114**, 497 (1925)
30. Conrad and Reinbach, Ber. **35**, 1816 (1902)
31. West, J. Chem. Soc. **125**, 1279 (1924)
32. Organic Syntheses, Vol. II, p. 75
33. Organic Syntheses, Vol. VII, p. 8

34. Organic Syntheses, Vol. VII, p. 9
35. Adiches, Ber. 63, 2758 (1930)
36. Conrad, Ann. 188, 218 (1877)
37. Bauer, Ann. 229, 165 (1885)
38. Steinkopf, Ber. 41, 2541 (1908)
39. Organic Syntheses, Vol. VII, p. 34
40. Organic Syntheses, Vol. VII, p. 78
41. Sörensen, Chem. Zentr. (1903) II, 33
42. Organic Syntheses, Vol. I, p. 15
43. Kohler, Amer. Chem. J., 42, 381 (1909)
44. Organic Syntheses, Vol. X, p. 48, Vol. XI, p. 102
45. Freund, Ber. 17, 133 (1884)
46. Jörgensen, J., prakt. Chem. [2] 19, 44 (1879)
47. Jörgensen, Z. anorg. Chem. 17, 463 (1898)
48. Duval, Ann. Chim. [10] 18, 263 (1932)
49. Willard and Hall, J. Amer. Chem. Soc. 44, 2220 (1922)
50. Jörgensen, Z. anorg. Chem., 2, 283 (1892)